Summary of the Office Action

1. The rejection of claims 28 and 32-35 under 35 U.S.C. 112 (first paragraph) was withdrawn.

2. The statutory double-patenting rejection under 35 U.S.C. 101 of claims 30-31 was withdrawn.

3. All of the prior art rejections were withdrawn.

4. Claims 28 and 30-31 remain rejected under the judicial doctrine of obvious-type double patenting as claiming the same invention as that of claims 1 & 3 of U.S. patent 6,028,174.

5. Claims 38 and 39 were rejected under 35 U.S.C. 112 (second paragraph) as being indefinite for use of the term "glial derived" in claim 38.

6. Claims 21-39 were rejected under 35 U.S.C. 112 (first paragraph) as containing subject matter which was described in the specification in such a way as to enable the skilled artisan to make and use the invention.

Response to the Office Action

As previously discussed in the telephonic interview on April 12, 2001 and as set forth in the Amendment filed July 20, 2001, Applicants agreed to submit a terminal disclaimer to overcome the obvious-type double patenting rejection of claims 28 and 30-31. Applicants respectfully request that this rejection be held in abeyance until such time that allowable subject matter is found with the understanding that a disclaimer will be provided at that time.

Claims 38 & 39 were rejected under 35 U.S.C. 112 (second paragraph) for purportedly being indefinite for use of the term "glial-derived" in claim 38. Applicants have amended claim 38 to substitute the term "glial in origin" for "glial-derived" in claim 38. Applicants bring to the attention of the Examiner that this same language was allowed by this Examiner in related divisional application 09/980,394 (now U.S. Patent 6,319,891). In light of the claim amendment and aforementioned remarks, Applicants respectfully request that the rejection be withdrawn.

Rejections based on 35 U.S.C. 112 (first paragraph)

Claims 21-39 were rejected under 35 U.S.C. 112 (first paragraph) as purportedly containing subject matter which was not described in the specification in such a way as to enable the skilled artisan to make and use the invention. The Office Action indicates that there is no objective evidence that the claimed pharmaceutical composition can readily be used in humans because no experimental data is presented indicating that the chlorotoxin peptide actually crosses the blood-brain barrier.

In response to this rejection, Applicants submit the Rule 1.132 Declaration of Dr. Vernon Alvarez, an expert in the field of peptide chemistry and pharmaceutics, which demonstrates that a pharmaceutical composition containing the chlorotoxin peptide crosses the blood-brain barrier and targets glioma cells. Applicants specifically bring to the attention of the Examiner that radiolabeled chlorotoxin, when administered parentally in mice via intravenous tail vein injection, crosses the blood-brain barrier and targets glioma cells implanted in the right hemisphere of the cerebral cortex of nude mice. Applicants further submit that the *in vivo* murine model used to demonstrate penetration of the blood brain barrier could readily be extrapolated by the skilled artisan to ascertain that the chlorotoxin peptide in the claimed pharmaceutical composition would readily pass the blood-brain barrier in humans following parental administration.

Applicants also bring to the attention of the Examiner claims 1 to 3 in U.S. Patent 6,319,891 which were allowed by the Examiner as shown below.

1. A method of treating a tumor expressing a glioma chloride channel in a patient comprising administering an effective amount of a pharmaceutical composition comprising chlorotoxin linked to a cytotoxic agent.

2. The method of claim 2 wherein the tumor is glial in origin.

3. The method of claim 3 wherein the tumor is a glioma.

Applicants submit that certain issued claims, for instance claim 3, encompass but are not limited to a method of treatment which requires penetration of the blood-brain barrier by the pharmaceutical composition comprising chlorotoxin just as in the present application. In view of

the attached declaration, aforementioned issued claims and remarks, Applicants respectfully request that the rejection be withdrawn.

Conclusion

The foregoing amendments and remarks are being made to place the application in condition for allowance. Applicants respectfully request reconsideration and the timely allowance of the pending claims. A favorable action is awaited. Should the Examiner find that an interview would be helpful to further prosecution of this application, they are invited to telephone the undersigned at their convenience.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned "Version with markings to show changes made" as required by the amended rules.

If there are any additional fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 50-0310. If a fee is required for an extension of time under 37 C.F.R. 1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted
Morgan, Lewis & Bockius LLP

Dated: **January 24, 2001**
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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

Claim 38 has been amended as follows:

38. (Once Amended) A pharmaceutical composition comprising a pharmacologically effective dose of chlorotoxin and a cytotoxic moiety that is effective to suppress the growth of [~~glial-derived neoplastic cell~~] tumor cells which are glial in origin.